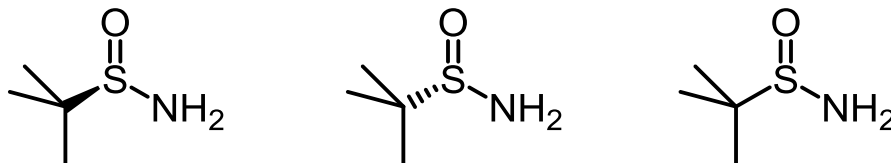


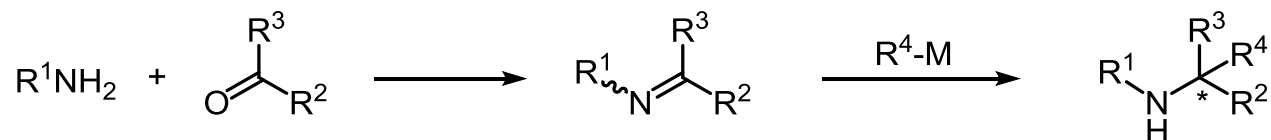
Reagent of the Day

Ellman's Sulfinamides (*tBs*)



Celine Santiago
July 31, 2017

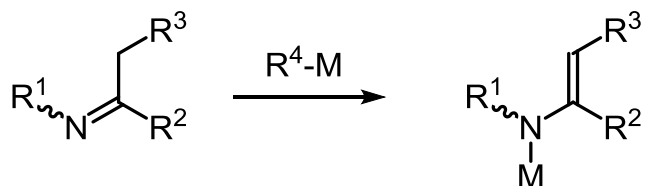
Asymmetric Synthesis of Amines



Factors affecting successful nucleophilic addition to imines

- Steric and electronic properties of the *N*-substituent
- *N*-substituent prevents rapid imine oligomerization
- Majority of *N*-substituted imines are unstable or inconvenient to store

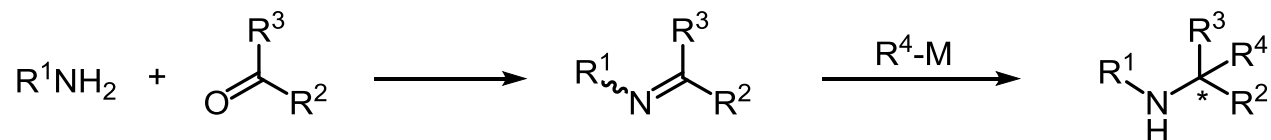
α -deprotonation



Possible Solutions

- Modulating the electronic properties of the *N*-substituent can provide stable compounds
- When reacted with basic nucleophiles, EW *N*-substituents are necessary to activate imines

Asymmetric Synthesis of Amines



R^1 = *p*-tolyl (Davis), *tert*-butyl (Ellman)
 M = Li, MgBr

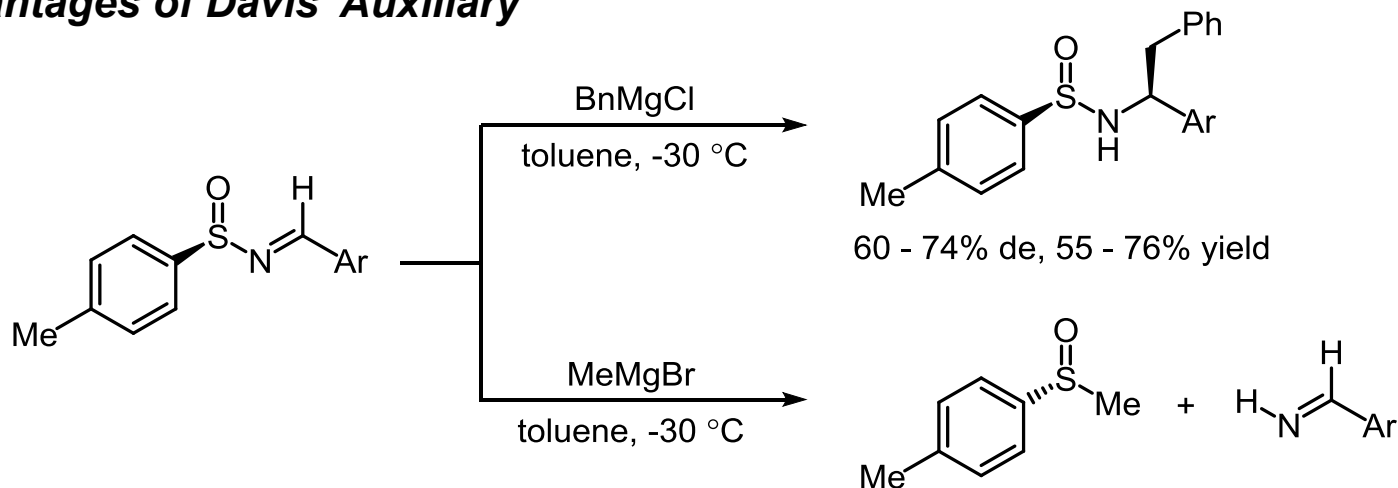
R^4 = alkyl, aryl, heteroaryl
 R^2, R^3 = H, alkyl, aryl, heteroaryl

Sulfinyl group as an ideal auxiliary

- Activates imine for nucleophilic addition
- Provides diastereofacial selectivity
- Easy to remove by treatment with mild acid

Davis' *N*-*p*-toluenesulfonyl substituent

Disadvantages of Davis' Auxiliary



With Ellman's Auxiliary

Ar = Ph

(88% yield, dr 97:3)

Limitations

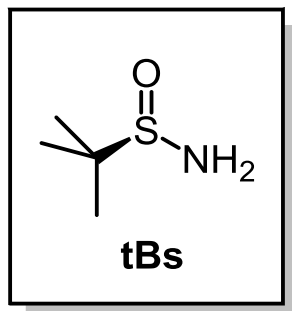
- *p*-toluene-sulfinamide is a poorer nucleophile
- does not cleanly condense with aldehydes
- Preparation routes proceed in modest yields

Davis, *J. Org. Chem.* **1997**, 62, 2555.

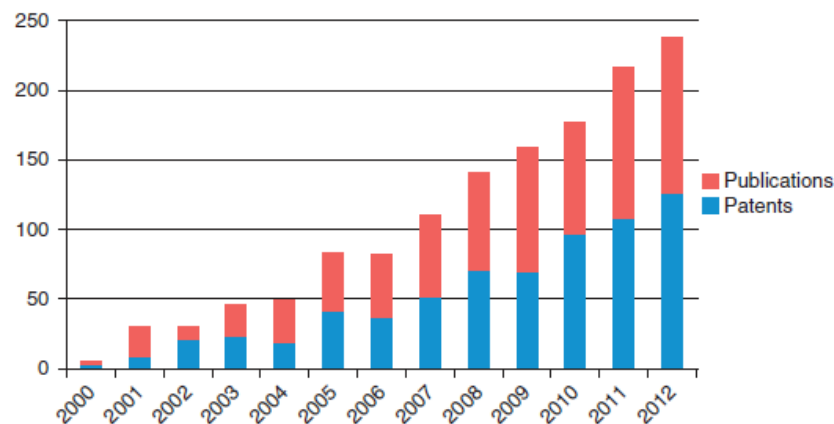
Ellman, *J. Am. Chem. Soc.* **1997**, 119, 9913.

Ellman, *Acc. Chem. Res.* **2002**, 35, 984.

Ellman's Sulfinamide



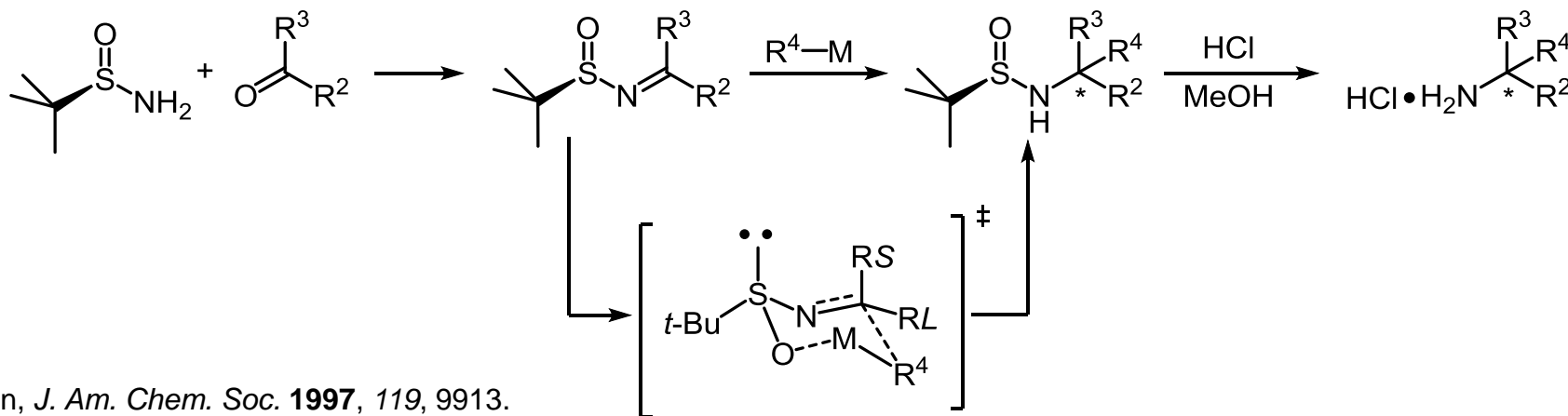
Citations of tBs and its derivatives



Advantages

- Enhances the nucleophilicity of the amine
- Minimizes competitive nucleophilic attack at sulfur
- Higher diastereofacial selectivity
- Preparation route is higher yielding; mole scale

General Reaction Scheme

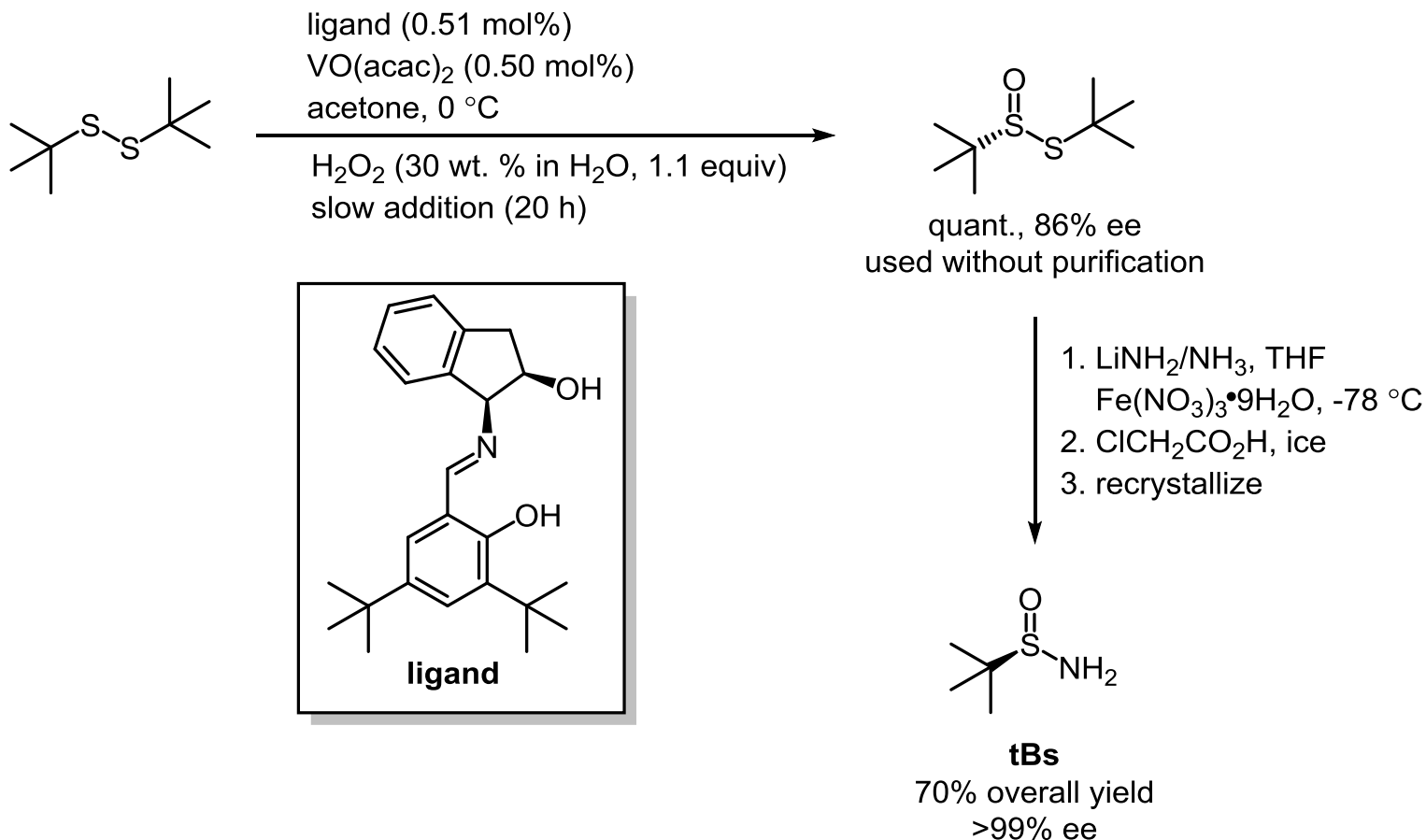


Ellman, *J. Am. Chem. Soc.* **1997**, 119, 9913.

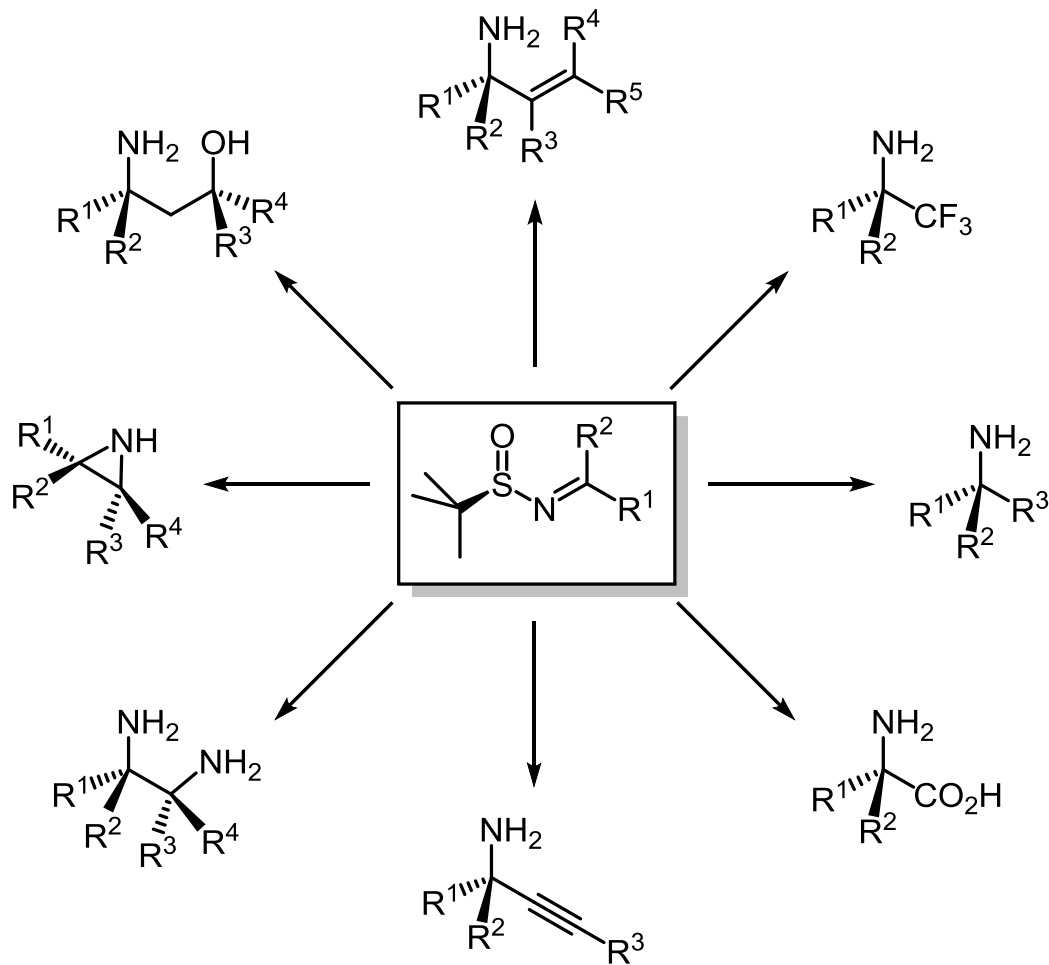
Ellman, *Acc. Chem. Res.* **2002**, 35, 984.

Ellman, *Nat. Protoc.*, **2013**, 8, 2271.

Optimized Synthesis of *tert*-butanesulfinamide (*t*Bs)



A Versatile Intermediate to Access Chiral Amines



Application to Pharmaceuticals

